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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	9

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/887,052	MOECKEL ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-87* is/are pending in the application.

4a) Of the above claim(s) *11-17, 20-23, 26-29,32-35,42-82, 85-87* is/are withdrawn from consideration.

5)☐ Claim(s) *1,3,4,18,19,24,25,30,31,36,38,83 and 84* is/are allowed.

6)☐ Claim(s) *2,5-10,37 and 39-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-87 are at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-10, 18, 19, 24, 25, 30, 31, 36-41, 83 and 84, in Paper No. 7 is acknowledged. The traversal is on the ground(s) that the claims of Groups IX, XII, XV, and XVI are directly dependent from the claims of Group I and as such these groups are not separable. As stated previously, Groups I and Groups IX, XII, XV, and XVI are related as product and processes of use, and as the product of Group I can be used in a materially different process than those of Groups IX, XII, XV, and XVI, the inventions are thus distinct and restrictable. Applicants further traverse the restriction requirement on the basis that a search of all claims would not constitute a serious burden on the Office, particularly as many of the restricted Groups are classified in the same subclasses or in the case of Groups !, V and VI are each drawn to polypeptides having a -subunit of RNA polymerase activity. This argument is not found persuasive for the following: While the searches for many of the groups overlap, they are not coextensive. For example, search of Group II would require a search of subclass 530/350, a search of Group IX would require search of subclass 435/106, a search of Group XII would require search of subclass 435/6. A search of each of these subclasses would be unnecessary the search of the elected group I. Further Groups I, V and VI are each drawn to structurally different

polynucleotides, that are not capable of use together as previously stated and are thus distinct and restrictable. Applicants reference to rejoinder is acknowledged and will be dealt with at the time that an allowable product claim is determined.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11-17, 20-23, 26-29, 32-35, 42-82 and 85-87 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 7.

Priority

Applicants claim of priority to German Application No. DE10107229.5, filed February 16, 2001, is acknowledged. It is further noted that a certified copy of this priority document is present in the application file.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosures, Paper No. 8, filed 12/6/2002, is acknowledged., however many of the references are missing. Those present and considered have been initialed.

Claim Objections

Claims 37 and 39 are objected to because of the following informalities:

Claims 37 and 39 each recite specific stains of *Corynebacterium,* and *Brevibacterium* (i.e. FERM 1079, FERM-P 1708, FERM-P1712, FERM-P6463, FERM-P6464, DM58-1, DG 52-5, DSM 5714 and DSM-12866.). In some recitations, such as FERM-P 1708, applicants include a "space" between "P" and "1708", where as in others, such as FERM-P1712, applicants do not. This is not consistent with the specification on page 9, lines 26-34. It is suggested that applicants maintain consistency throughout the specification including the claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 9, 40 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 9 are each indefinite in that they recite "...a protein having the activity of the β-subunit of RNA polymerase B." It is unclear what "activity of the β-subunit of RNA polymerase" applicants refer. A biologically active protein may

encompass a variety of different biological activities. These include but are not limited to immunological activity, such as acting as an antigen for an antibody; regulatory activity, such as that exhibited by many proteins which control transcription and/or translation of not only their encoding nucleic acids but other nucleic acids as well; or enzymatic activity, for example, RNA polymerase activity. It is not clear what is encompassed by the "activity" of β-subunit of RNA polymerase B and if includes biological activities in addition to enzymatic activity.

Claim 40 (41 dependent on) is indefinite in that it is unclear in that it is drawn to "A Coryneform bacterium which comprises an enhanced rpoB gene." Specifically it is unclear in what an "enhanced rpoB gene" is and what it encompasses.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5-9 are directed to all possible polynucleotides which are at least 70%, 80% or 90% identical to the polynucleotide of claim 3, (SEQ ID NO: 1) (claims 5-8) and all possible polynucleotides which hybridize under stringent conditions of 5X SSC at a temperature from 50 to 68°C. Claim 10 is directed to all possible polynucleotides which

comprises at least 15 consecutive nucleotides of the polynucleotide of claim 3 (SEQ ID NO: 1). The specification, however, only provides a single representative species of polynucleotide (i.e. SEQ ID NO: 3) encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these enzymes by any identifying structural characteristics or properties. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 5-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide which encodes a protein having the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for any polynucleotide which comprises a mere 15 consecutive nucleotides of SEQ ID NO: 3 or is 70-90% identical to SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-5 are so broad as to encompass any polynucleotides which is at least 70%, 80% or 90% identical to the polynucleotide of claim 3, (SEQ ID NO: 1) (claims 5-8) and any polynucleotide which hybridizes under stringent conditions of 5X SSC at a temperature from 50 to 68°C. Claim 10 is so broad as to encompass any polynucleotides which comprises at least 15 consecutive nucleotides of the polynucleotide of claim 3 (SEQ ID NO: 1). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, place insufficient structural and no functional limits on the claimed polynucleotides. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which

the proteins' structure relates to its function. The same is true of a polynucleotide sequence, as the nucleic acid sequence of the polynucleotide directly correlates with the amino acid sequence of the polypeptide. However, in this case the disclosure is limited to a polynucleotide which encodes a protein having the amino acid sequence of SEQ ID NO: 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a polynucleotides sequence where nucleic acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any polynucleotide and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given polynucleotide to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass those polynucleotides having the claimed structural relationship to SEQ ID NO: 1, because the specification does not establish: (A) regions of the polynucleotide structure which may be modified without effecting the desired activity; (B) the general tolerance of the claimed polynucleotides to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue of SEQ ID NO: 1 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the

extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polynucleotides of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polynucleotide with the claimed structural relationship to SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 37 and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention of claims 37 and 39 appears to employ novel strains of *Corynebacterium,* and *Brevibacterium*(i.e. FERM 1079, FERM-P 1708, FERM-P1712, FERM-P6463, FERM-P6464, DM58-1, DG 52-5, DSM 5714 and DSM-12866.) Since these strains are essential to the claimed host cells, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. These organisms are not fully disclosed, nor have they been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the specific strains of *Corynebacterium,* and *Brevibacterium*.. Accordingly, it is deemed that a deposit of these stains should have been made in accordance with 37 CFR 1.801-1.809.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5, 8 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Imboden et al. (Database EMBL on line, Accession No. U12205.1, March 2000).

Imboden et al. teach the rpoB gene of Mycobacterium tuberculosis which comprises a polynucleotide that has a best local similarity score of at least 71% and comprises many regions of at least 15 consecutive nucleotides of SEQ ID NO: 1. Thus claims 5, 8 and 10 are anticipated by Imboden et al.

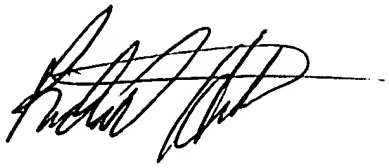
Claims 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Honore et al. (Database EMBL on line, Accession No. Z14314, Feb 1993, See IDS ref AR).

Honore et al. teach the rpoB gene of *Mycobacterium leprae* which comprises a polynucleotide that has comprises many regions of at least 15 consecutive nucleotides of SEQ ID NO: 1. Thus claim 10 is anticipated by Honore et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
December 23, 2002